REMARKS

In response to the final Office Action of October 25, 2004, Applicants have amended the claims, which, when considered with the following remarks, is deemed to place the present application in condition for allowance or else in better condition for appeal. Favorable consideration of all pending claims is respectfully requested. This amendment was previously submitted on April 21, 2005, but was not entered by the Examiner because Applicants' representative inadvertently failed to sign the last page of the "Remarks" section. The present amendment is identical in all respects to the amendment submitted on April 21, 2005, except that it has been re-dated and the final page of the Remarks section is signed by Applicants' representative. A re-dated Amendment Transmittal form is also submitted. Copies of the petition for extension of time and Notice of Appeal which papers are not re-dated are also submitted herewith, both of which papers are marked: "previously paid" and "previously submitted". A copy of the checks previously submitted is also submitted herewith.

In the Office Action of October 25, 2004, the Examiner has indicated that the specification of the present application should be updated with respect to the relationship to the parent application that has matured into a U.S. patent. By this amendment, the section entitled "CROSS REFERENCE TO RELATED APPLICATIONS" has been amended to reflect that parent application Serial No. 09/077,354 is now U.S. Patent No. 6,255,096.

Claim 20 remains rejected under 35 U.S.C.§ 112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. According to he Examiner, the metes and

bounds of the phrase "or other convenient means" are not clear. In order to advance prosecution of this application, and not meant as an acquisition to the position of the Examiner, the language "or other convenient means" has been deleted from claim 20. Withdrawal of the rejection of Claim 20 under 35 U.S.C. §112, second paragraph is therefore respectfully requested.

Claims 19-27, 29-31, 35-36, and 60-64 remain rejected under 35 U.S.C. §102(b) as allegedly anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as allegedly obvious over Sasaki et al. (1991) *J. Biochem. 110*(5): 842-846. The Examiner has based the rejection on the public availability of a printed publication reporting the purification of the enzyme from various tissue sources. *See* October 25, 2004 Office Action, page 3, final sentence.

Sasaki et al. (1991) has been cited for teaching purification of a human NAG from human liver. The reference has also been cited for teaching that the enzyme is 80 kDa when tested by SDS/PAGE and that a deficiency of the enzyme is known to cause MPS IIIB or Sanfilippo B syndrome, a severe neurodegenerative disease in humans.

The Examiner has taken the position that the enzyme disclosed in the reference and that claimed in the present invention are inherently one and the same and that Applicants have not done anything to the enzyme except to isolate the recombinant form of the purified enzyme disclosed in the reference. As stated in line 6, page 5, of the Office Action, the Examiner sees no material, structural, or functional difference between the purified enzyme disclosed in Sasaki et al. (1991) and the purified recombinant enzyme disclosed and claimed by Applicants.

On page 5, lines 10-15, the Examiner has asserted that the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. In addition, on page 7, first full paragraph of the October 25, 2004 Office Action, the Examiner has made a number of assertions, each of which Applicants address below.

With respect to Applicants meeting their burden, it is respectfully submitted that Applicants have previously demonstrated both a novel and unobvious difference between the claimed product and that of the prior art. Applicants previously submitted and reiterate such submission that the presently claimed α-N-acetylglucosaminidase is produced recombinantly and yields an enzyme having about an 89kDA and about 79 kDa molecular weight as determined by SDS PAGE. As presently amended, claims 19 and 60, and claims dependent therefrom, recite that the recombinant α-N-acetylglucosaminidase is "produced in a cell capable of N-glycosylating said α-N-acetylglucosaminidase".

On page 7, first paragraph, the Examiner has posited the following:

> The argument regarding the molecular weight is also highly misplaced. This is because the difference in the molecular weights between the claimed enzyme and that in the reference is not significant. Furthermore, it is well known in the art that there is always a slight variation during molecular weight determinations. The claimed molecular weight is "about 89 kDa" and "about 79 kDa", while the molecular weight recited in the reference is "about 82 kDa" and "about 77 kDa". It can be readily seen that the differences in the molecular weight are not significant and concluded that it is due to experimental error.

Applicants respectfully submit that the difference in the molecular weights between the claimed enzyme and the tissue-derived enzyme disclosed in Sasaki et al. is certainly significant. In the first instance, the molecular weight of human liver-derived α-N-acetylglucosaminidase as reported by Sasaki et al. (1991) is 80 kDa as determined by SDS PAGE. *See* Sasaki et al. (1991), abstract and page 845, column 2, fourth full paragraph. In contrast, Applicants' claims recite a recombinant α-N-acetylglucosaminidase having a molecular weight of about 89kDa and about 79 kDa as determined by SDS PAGE. Thus, a major distinguishing feature of the present invention is the 89 kDa form of the enzyme, as well as the 79 kDa form, which forms Sasaki et al. do not disclose.

Moreover, it is Applicants, *not* Sasaki et al., who first disclosed molecular weights, of placenta-derived α-N-acetylglucosaminidase being 82 kDa and 77kDa. *See* present application, page 36, Examples 1 and 2, and Figure 1. Thus, contrary to what the Examiner has stated on page 7 of the Office Action, there is no molecular weight of "about 82 kDa and about 77 kDa" disclosed in Sasaki et al.

On page 7, second paragraph, of the Office Action, the Examiner has stated that "Applicants have not shown a material, structural, or functional difference/s between the purified enzyme and the recombinant enzyme. Absent such information, the purified protein inherently possesses all the characteristics of the recombinant enzyme even though the reference is not explicit about those characteristics."

In response to this position of the Examiner, it is submitted that a showing of material and structural difference between the purified enzyme and the recombinant enzyme has been made in this application. For example, in the amendment submitted on

August 9, 2004, Applicants provided a copy of Weber et al. (2001) *Protein Expression and Purification 21*:251-259, and directed the Examiner to page 255, column 1. *See* Amendment submitted August 9, 2004, page 10, second paragraph. That section of Weber et al. is reproduced below:

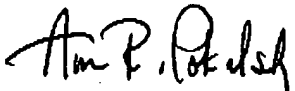
> SDS-PAGE showed two bands of approximately 79 and 89 kDa, with the 79 kDa form enriched but not exclusively eluted by 50 mM NaCl from the DEAE-column while the 89 kDa form eluted preferably with higher salt concentrations (Fig. 1). It had not been possible to separate both forms, even if other matrices were used. Previously purified NAGLU had reported molecular masses of 82 kDa for enzyme isolated from human fibroblasts with precursor and intermediate or mature forms ranging from 86 kDa to 77 and 73 kDa (5), whereas for NAGLU purified from human kidney carcinoma cells had an apparent molecular weight of 80 kDa (6). A secreted 86-kDa from was observed in the medium of these cells (7) and isolated from urine (8).
>
> The two forms of NAGLU, purified from human placenta with apparent molecular weights of 77 and 80 kDa (10) were differentially eluted with buffer compositions similar to the two forms of recombinant enzyme. The placenta isoforms represent mature enzyme and precursor that differ by 36 amino acids trimmed off the N-terminus. Whereas, the two forms of recombinant enzyme seem to differ in posttranslational modifications of N-glycosylation moieties. D glycosylation with PNGaseF reduced the apparent molecular weight of both forms to approximately 70 kDa (Fig. 1), indicating that the difference in size of the two rNAGLU forms was due to carbohydrate moieties rather than N-terminal processing of the NAGLU polypeptide.

Thus, Applicants have done more than obtained a purified protein as a recombinant enzyme. Applicants have shown that the presently recited form of the enzyme, i.e., produced in a cell capable of N-glycosylation and having a molecular weight of about 89 kDa and about 79 kDa, is structurally different from the liver-derived form of NAGLU disclosed by Sasaki et al. since the claimed enzyme exhibits a different

glycosylation pattern than does a tissue-derived form of the enzyme. As such, the presently claimed NAGLU is distinguished from, and unobvious over, the teachings of Sasaki et al., and withdrawal of the rejection of claims 19-27, 29-31, 35-36, and 60-64 under 35 U.S.C. §102(b) and/or 35 U.S.C. 103(a) is warranted.

In view of the foregoing remarks and amended claims, it is firmly believed that the present application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,



DILWORTH & BARRESE, LLP
333 Earle Ovington Boulevard
Uniondale, New York 11553
Tel. No. (516) 228-8484
Fax No. (516) 228-8516
ARP:ml

Ann R. Pokalsky
Registration No. 34,697
Attorney for Applicants